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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,385	11/23/2001	Koji Yanai	2001-1611	4331

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	6

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,385	YANAI ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-26 and 50-52* is/are pending in the application.

4a) Of the above claim(s) *26 and 50-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *NA* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 22-26 and 50-52 are still at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, Claims 22-25 in Paper No. 5 is acknowledged.

Claims 26 and 50-52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

Applicants amendment of the first line of the specification to state that this application is a Divisional application of Serial No. 09/142,623, filed September 10, 1998, now allowed, which is a 371 of PCT/JP97/00757, filed March 11, 1997, which is pending is acknowledged. Applicants statement that PCT/JP97/00757 is pending is confusing and it is requested that applicants clarify this statement.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the

list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure, filed 11/23/2001 is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

On page 7 in the under the Brief Description of the Drawings, applicants refer to Figure 4 and Figure 5, wherein both Figures 4 and 5 each comprise a Figure 4A and Figure 4B. It is suggested that the description of these figures be amended to reflect this.

On page 37, line 6, applicants misspell "transformants" as "transtormants".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 (23-25 dependent on) is indefinite in that the limitation "without β-fructofuranosidase activity" is unclear. Applicants claim is drawn to an *Aspergillus* mold fungus without β-fructofuranosidase activity, however as applicants have not disclosed the β-fructofuranosidase activity of the disclosed mutant *Aspergillus niger* NIA1602, it is unclear what applicants consider to be encompassed by "without β-fructofuranosidase activity". Literal interpretation of the referred to limitation means "no activity", however it is believed that this is not applicants intent as it is believed that applicants disclosed *Aspergillus niger* NIA1602 has some β-fructofuranosidase activity, however reduced relative to wildtype. For the purpose of advancing prosecution, claim 22 is interpreted as being drawn to a mutant *Aspergillus* mold fungus with significantly reduced β-fructofuranosidase activity relative to its wildtype.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 22 and 24 are directed to all possible *Aspergillus niger* mold fungi without β-fructofuranosidase activity (See also above 112 second paragraph rejection). The specification, however, only provides a single representative species encompassed by

these claims, the mutant *Aspergillus niger* NIA1602 (FERM BP-5853), wherein the mutant Aspergillus niger has been mutated such that its β-fructofuranosidase gene is deleted. The specification also fails to describe additional representative species of the claimed *Aspergillus niger* mold fungi by any identifying structural characteristics or properties other than being "without β-fructofuranosidase activity" recited in claims 22, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 22 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant *Aspergillus niger* in which its β-fructofuranosidase gene has been deleted, does not reasonably provide enablement for any *Aspergillus niger* without β-fructofuranosidase activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir.

1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 22 and 24 are so broad as to encompass any *Aspergillus niger* without β-fructofuranosidase activity. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of *Aspergillus niger* mutants broadly encompassed by the claims, including any mutant *Aspergillus niger* which has reduced β-fructofuranosidase activity relative to its wildtype (See above 112 second paragraph rejection). As the claims rejected under this section of U.S.C. 112, first paragraph, place only a functional limit on the claimed *Aspergillus* mutants and applicants have only disclosed a single means of achieving the claimed Aspergillus with the claimed functional limit, applicants have not enabled the full scope of the genus of any mutant *Aspergillus niger*, wherein said mutant does not have β-fructofuranosidase activity.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function.

However, in this case the disclosure is limited to those mutant Aspergillus mutants in which the b-fructofuranosidase gene is deleted.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all Aspergillus niger mutants without β-fructofuranosidase activity because the specification does not establish: (A) regions of the protein structure which may be modified without effecting β-fructofuranosidase activity; (B) the general tolerance of β-fructofuranosidases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a β-fructofuranosidase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to delete the β-fructofuranosidase activity as claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well

understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those mutant *Aspergillus niger* fungi of the claimed genus without β-fructofuranosidase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any *Aspergillus niger* without β-fructofuranosidase activity. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those mutants having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention of claim 25 appears to employ a novel strain of an isolated *Aspergillus niger* NIA1602 (FERM BP-5853). Since the *Aspergillus niger* fungus isolate is claimed, it must be obtainable by a repeatable method set forth in the specification or

otherwise be readily available to the public. The organism is not fully disclosed, nor has it been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the *Aspergillus niger* NIA1602 (FERM BP-5853).

It is noted that applicants have deposited the organism but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
4. the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by Nakamura et al. (Journal of Fermentation and Bioengineering, Vol 78, No. 2, 134-139, 1994, See IDS, Ref AL).

Nakamura et al. teach the occurrence of two forms of extracellular endoinulinase from *Aspergillus niger* mutant 817. Nakamura et al. create, screen for and isolate the *Aspergillus niger* mutant 817, which was selected based on its increased inulinase and reduced invertase activity. The *Aspergillus niger* mutant 817 showed reduced invertase activity compared to the wild-type (see Table 1, page 137). Thus claims 22 and 24 are anticipated by Nakamura et al. (See above 112 second paragraph rejection).

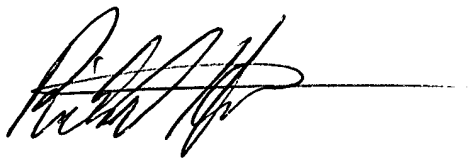
Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



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Art Unit 1652
April 4, 2003